IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

J.B.D.L. Corp. d/b/a BECKETT APOTHECARY, et al., **Plaintiffs,** **v.** **WYETH-AYERST LABORATORIES, INC., et al.,** **Defendants.**	**Civil Action No. C-1-01-704** **Judge Sandra S. Beckwith** **Magistrate Judge Timothy S. Hogan**
CVS MERIDIAN, INC. AND RITE AID CORP., **Plaintiffs,** **v.** **WYETH,** **Defendant.**	**Civil Action No. C-1-03-781** **Judge Sandra S. Beckwith**

DEFENDANTS' MOTION TO PROHIBIT PLAINTIFFS FROM INTRODUCING CERTAIN EVIDENCE BASED ON THE TESTIMONY OR ANALYSIS OF DR. PHILLIP SARREL

Defendants Wyeth Pharmaceuticals (formerly known as Wyeth-Ayerst Laboratories, Inc.) and Wyeth (formerly known as American Home Products Corporation) (collectively "Wyeth") through its attorneys, hereby respectfully move this Court to prohibit Plaintiffs J.B.D.L. Corporation, et al., and CVS Meridian, Inc. and Rite Aid Corporation (collectively "plaintiffs") from introducing certain evidence based on the testimony or analysis of Dr. Phillip Sarrel. In support of this motion, Wyeth submits and incorporates the attached memorandum of law.

Dated: May 13, 2005

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MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION TO PROHIBIT PLAINTIFFS FROM INTRODUCING CERTAIN EVIDENCE BASED ON THE TESTIMONY OR ANALYSIS OF DR. PHILLIP SARREL

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INTRODUCTION AND SUMMARY

This motion seeks to exclude three discrete areas of testimony by plaintiffs' physician expert (Dr. Phillip Sarrel) pursuant to *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 592-93 (1993).

Premarin is an estrogen therapy ("ET") prescription pharmaceutical product that Wyeth has manufactured and marketed for over 60 years. It is classified as a "conjugated estrogens" product[1] and is approved by the Food and Drug Administration ("FDA") for the treatment of vasomotor symptoms (i.e., hot flashes) and various other indications. Premarin has enjoyed a long clinical history of successful use and has been the subject of over 3,000 studies.[2] Cenestin – which is a branded synthetic "conjugated estrogens" prescription product – was approved by the FDA for the single indication of vasomotor symptoms in 1999.

The fundamental issue in this case is whether Wyeth's rebate agreements with managed care organizations (MCO's) prevented other ET products (including Cenestin) from obtaining access to MCO formularies and thereby foreclosed them from the market for ET products. In determining the reasons for the relative market success of Premarin or Cenestin, an issue that the fact-finder is likely to consider is the comparative benefits of these (and other) ET products. Wyeth will submit substantial evidence at trial that Cenestin's limited success in obtaining formulary listings was not the result of Wyeth's rebate agreements, but instead was largely attributable to Cenestin's lack of therapeutic

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1 FDA Response to Wyeth-Ayerst Citizen Petition (March 24, 1999) (Exh. 1).

2 Press Release, Wyeth-Ayerst, Uniqueness of Premarin (conjugated estrogens tablets, USP) Confirmed (March 25, 1999), at WYE 021501 (Exh. 2).

indications, its lack of several dosage strengths, and the small number of clinical studies related to the product. In response, plaintiffs have hired Dr. Phillip Sarrel, a Yale University Professor and the Chairman of the medical consulting board of Cenestin's manufacturer, to express his views that Cenestin is a better ET product than Premarin. Wyeth intends to rebut Dr. Sarrel's testimony by evidence and cross-examination at trial. However, certain discrete areas of Professor Sarrel's proposed testimony cross the line under *Daubert* and should be excluded from the jury.

1. *Testimony Regarding Estrogen Levels in Each Premarin Pill.* Dr. Sarrel intends to testify that Cenestin is better than Premarin because Cenestin delivers a uniform amount (and balance) of estrogens with every pill, while different Premarin pills supposedly contain different quantities of estrogens, due to the fact that they are supposedly made from different "batches of horse urine." (Sarrel Rep. ¶¶ 27-28 (Exh. 4).) Such testimony is derived from a false premise: There is no evidence that each Premarin pill is made from a single batch of horse urine; nor is there any evidence from which Dr. Sarrel could legitimately opine on the extent, if any, to which the estrogen levels in Premarin pills vary, or whether that variance is any different from the variance in Cenestin pills.

2. *Testimony Regarding Dissolution of Premarin Pills.* Dr. Sarrel states that "[v]arious dissolution tests have shown that when Premarin is ingested, the estrogens that are released have peak levels and then dip into a trough" (Sarrel Rep. ¶ 31 (Exh. 4)) and that these peaks and troughs contribute to persistent symptoms and side effects. (*Id.* ¶¶ 31, 33.) Based on this premise, he opines that "Cenestin offers a distinct advantage over Premarin in the area of dissolution and absorption." (*Id.* ¶ 34.) In fact, there is *no*

empirical basis for differentiating between the absorption profiles of Cenestin and Premarin in human beings; the article upon which Dr. Sarrel relies – which did not even address dissolution in humans – expressly acknowledges that no "clinical implications" of the laboratory differences have been demonstrated.

3. *Testimony Regarding Beliefs of Other Doctors.* Notwithstanding his lack of any training in this area, Dr. Sarrel intends to opine on the effects of formulary management (including exclusion from formularies) on the willingness of doctors to prescribe ET products. According to Dr. Sarrel, "[m]any, if not most of the physicians I have spoken with are effectively limited to the drugs listed on the [managed care] formularies." (Sarrel Rep. ¶ 51 (Exh. 4).) He opines that "[w]hen non-formulary alternatives are allowed, there usually is a process requiring a formal request and approval by the pharmacy review board of the [MCO]" (*id*.) and that many physicians may believe formulary status is a "stamp of approval" when in fact it "may simply reflect" a restrictive agreement between a MCO and the drug's manufacturer. (*Id*. ¶ 52.)

Yet Dr. Sarrel has no basis for making such sweeping generalizations. He admits that his own personal experience has been to the contrary; that he is generally ignorant of formulary management; and that his opinion is based not on any scientific basis, but on random conversations with other physicians. Dr. Sarrel is not an expert on formulary management and his testimony on these issues should be excluded.

Dr. Sarrel has no legitimate scientific basis or professional expertise that would enable him to offer expert testimony in these three areas. Rather, such testimony would amount to unvarnished and unsupported personal opinion and should be excluded by this Court as the "gatekeeper" of expert testimony. *Daubert*, 509 U.S. at 593.

ARGUMENT

To be admissible, expert testimony must (1) "assist the trier of fact," (2) be "based upon sufficient facts or data," (3) be "the product of reliable principles and methods," and (4) have "applied the principles and methods reliably to the facts of the case." Fed. R. Evid. 702. "If the witness is relying solely or primarily on experience, then the witness must explain how that experience leads to the conclusion reached . . . and how that experience is reliably applied to the facts. The trial court's gatekeeping function requires more than simply 'taking the expert's word for it.'" *Thomas v. City of Chattanooga*, 398 F.3d 426, 432 (6th Cir. 2005) (quoting Fed. R. Evid. 702 advisory committee's note). Furthermore, "an opinion based totally on incorrect facts will not speak to the case at hand and hence will be irrelevant." *Bradley v. Armstrong Rubber Co.*, 130 F.3d 168, 177 (5th Cir. 1997); *Guillory v. Domtar Indus.*, 95 F.3d 1320, 1331 (5th Cir. 1996). "An expert opinion that is based on scientifically valid principles will satisfy Fed. R. Evid. 702; an expert's subjective belief or unsupported speculation will not." *Smelser v. Norfolk S. Ry. Co.*, 105 F.3d 299, 303 (6th Cir. 1997) (citing *Daubert* (on remand), 43 F.3d 1311, 1316 (9th Cir. 1995).

I. DR. SARREL'S CLAIM THAT THE ESTROGEN LEVELS IN PREMARIN VARY SIGNIFICANTLY FROM PILL TO PILL IS UNFOUNDED AND SHOULD BE EXCLUDED.

According to his expert report, Dr. Sarrel intends to testify that Cenestin is superior to Premarin based in part on his belief that the levels of estrogens in individual Premarin tablets vary from pill to pill due to variances in estrogen levels in pregnant mares, from which Premarin is manufactured. (Sarrel Rep. ¶ 27 (Exh. 4).) But Dr. Sarrel is no expert on the manufacturing process of any ET product, let alone Premarin. Indeed,

Dr. Sarrel admitted at deposition that he *has no knowledge of the manufacturing process of Premarin.* (Sarrel Dep. at 146 (Exh. 3).) Instead, Dr. Sarrel has simply jumped to the conclusion that there are variances in estrogen levels of each "batch[ ] of horse urine" and therefore there are variances in estrogen levels of each Premarin pill. (Sarrel Rep. ¶ 27 (Exh. 4).) Nothing in the record supported this unfounded assumption, and Dr. Sarrel could offer no factual basis for jumping to this erroneous conclusion.

When Dr. Sarrel was confronted at deposition with the absence of any factual foundation for his testimony regarding the supposed variability of Premarin pills, he concocted an entirely different argument for why he believed Premarin pills varied more than Cenestin pills. He asserted that because the United States Pharmacopeia ("USP")[3] provides for acceptable "ranges" in estrogen levels in "Conjugated Estrogens," then the estrogen levels of Premarin pills can be assumed to vary to the maximum amount of the ranges in the USP. (Sarrel Dep. at 141-143 (Exh. 3).) Yet there is no more factual or scientific basis for this hastily substituted theory than for his erroneous assumption about Wyeth's process for manufacturing Premarin.

First, the variability standards in the USP merely establish the acceptable ranges of estrogen levels in "Conjugated Estrogens" pills. In other words, pills that fall within the ranges specified in the USP qualify as "conjugated estrogens." The USP's permissible ranges of estrogen levels for conjugated estrogens obviously do not constitute any evidence whatsoever that the actual estrogen levels in individual Premarin pills vary

[3] *See* 2005 U.S. Pharmacopeia Convention, Inc.: 2005 National Formulary, at 777-79 (2004) (Exh. 5). The USP is a publication of drug monographs, which give the specifications for the contents and dissolution of pharmaceutical products.

to the maximum extent permitted by the USP. In essence, Dr. Sarrel's assumption that Premarin pills vary in estrogen levels because the USP permits conjugated estrogens to fall within a range of estrogen levels is tantamount to the assumption that a specific driver varies between 40 miles per hour and 65 miles per hour on Interstate 275 simply because the speed limit allowed him to do so.

Moreover, as Duramed's own documents show, Cenestin pills must comply with the very same USP ranges for estrogen levels with which Premarin must comply.[4] Thus, it is utterly baseless for Dr. Sarrel to opine that Premarin pills are of greater variability than Cenestin pills based on the fact that both products must fall within exactly the same range of estrogen levels. Indeed, Duramed's own documents show that the estrogen contents of individual Cenestin pills vary, contrary to Dr. Sarrel's "impression" (Sarrel Dep. at 143) (Exh. 3)) that they are uniform in all Cenestin tablets. (Sarrel Rep. ¶ 28 (Exh. 4).)[5]

In sum, Dr. Sarrel is not competent to opine to the jury that individual Premarin pills vary in estrogen content to a greater degree than individual Cenestin pills. He is not an expert on Premarin's manufacturing process, and the permissible ranges of estrogen levels set forth in the USP are obviously not a factual basis for concluding that Premarin pills in fact have varying estrogen levels – let alone that these levels are more variable

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[4] Cenestin Product Monograph, at VIK 000914 (Exh. 6) (noting that the percentages of the different estrogens in Cenestin comply to the specifications for "Conjugated Estrogens USP"). The document claims that Duramed was developing a new monograph for "synthetic conjugated estrogens," but none has been published in the United States Pharmacopeia to date. *See U.S.* Pharmacopeia: 2005 National Formulary, at 772-781 (2004) (Exh. 5).

[5] Cenestin Product Monograph, at VIK 000914-15 Table 2 (Exh. 6).

than the estrogen levels in Cenestin. Expert testimony should not be allowed where, as here, "the testifying expert's opinion is too speculative" or "the underlying basis is faulty." *Walker v. Soo Line R.R. Co.*, 208 F.3d 581, 588 (7th Cir. 2000) (internal citations omitted) (citing *Wash. v. Armstrong World Indus.*, 839 F.2d 1121, 1123-24 (5th Cir. 1988) and *Nat'l Bank of Commerce v. Dow Chem. Co.*, 965 F. Supp. 1490, 1523-24 (E.D. Ark. 1996), *aff'd*, 133 F.3d 1132 (8th Cir. 1998) (per curiam)). Given the utter lack of any factual basis for Dr. Sarrel's "theory" that Premarin pills vary in estrogen levels more than do Cenestin pills, the Court should preclude Dr. Sarrel from testifying that Cenestin is in any way preferable to Premarin due to differences in "variability" from pill to pill.

II. DR. SARREL HAS NO BASIS FOR EXPERT TESTIMONY THAT PREMARIN is inferior to cenestin DUE TO Differences in their "dissolution" profiles

Dr. Sarrel's expert report states that "[v]arious dissolution tests have shown that when Premarin is ingested, the estrogens that are released have peak levels and then dip into a trough in the course of 24 hours." (Sarrel Rep. ¶ 31 (Exh. 4).) He claims these "dissolution failures" contribute to persistent symptoms and side effects. (*Id.* ¶¶ 31, 33-34.) Yet Dr. Sarrel's testimony is based upon a single article, which does not even address the dissolution of Premarin or Cenestin in the human body. Rather, the article simply addresses dissolution under laboratory conditions, and expresses no views at all about the relative "absorption" rates of Premarin and Cenestin into the human bloodstream. In fact, the very same article upon which Dr. Sarrel bases his "expert"

opinions about Premarin's dissolution in the human body concedes that any "clinical implications" of the laboratory findings "have yet to be fully elucidated."[6]

At his deposition, Dr. Sarrel agreed that there is *no empirical evidence* that any differences in dissolution between Cenestin and Premarin have any clinical effect. (Sarrel Dep. at 166-67 (Exh. 3).)[7] His theory that there are such clinical effects has admittedly not been subjected to peer review or publication. *See Daubert*, 509 U.S. at 593-94 (listing peer review and publication of theory as a factor for consideration under Rule 702). Dr. Sarrel is no expert on issues relating to Premarin's *in vivo* dissolution profile or its effects on humans, and he should not be permitted to offer expert testimony on this subject.

III. DR. SARREL SHOULD NOT BE ALLOWED TO OfFER EXPERT TESTIMONY CONCERNING MANAGED CARE FORMULARIES OR THEIR IMPACT UPON OTHER PHYSICIANS' PRESCRIBING PRACTICES

Plaintiffs also intend to have Dr. Sarrel testify that physicians generally avoid prescribing drugs that are not on MCO formularies. (Sarrel Rep. ¶¶ 49-60 (Exh. 4).) But

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[6] *See* Sarrel Dep. Exh. 5 (Henry M. Hess, Thomas C. Dowling & Michael J. Schwartz, *Clinical Implications of the Differences in Dissolution and Absorption Characteristics of Oral Estrogen Therapy Agents*, Today's Therapeutic Trends 94 (2003) (Exh. 7).) It also appears this article was written by a paid consultant to Duramed who did not disclose his affiliation in the article and that the article was not peer-reviewed. (Mallett Dep. at 75-76 (Exh. 8).)

[7] *See also* Tim Bonfield, *New Hormone-Replacer Called Better*, Cincinnati Enquirer, Feb. 3, 2001, at B9 (Exh. 9) (Dr. James Liu, director of the University of Cincinnati's division of reproductive endocrinology commenting: "I don't think anyone can say [that the different dissolution profiles has a 'clinical effect'], because there haven't been any studies."). In his deposition, Dr. Sarrel said that Cenestin's package insert – information required by the FDA to accompany the drug through the distribution chain – also supports his conclusions on dissolution and absorption. (Sarrel Dep. at 160 (Exh. 3).) But nowhere does Cenestin's package insert suggest that its dissolution and absorption profile has any clinical relevance. (*See* Sarrel Dep. Ex. 8, Cenestin Package Insert (Exh. 10).) Indeed, Dr. Hess' article confirms this fact. Hess et al., *supra*, note 6, at 94 (Exh. 7).

Dr. Sarrel admitted that he had not reviewed any literature concerning managed care formularies (Sarrel Dep. at 263 (Exh. 3)); that he had never taken any courses or done any study in the area of managed care formularies (*id*. at 98); that he did not even know what a "PBM" was (*id*. at 263); and that he did not know what a "tiered formulary" was (*id*. at 268). He could identify only one instance (involving a drug other than Premarin prescribed by groups of physicians in Poughkeepsie, New York and Madison, Wisconsin) to support his generalizations about physicians' need to lodge a "formal request" and obtain "approval by the [MCO] pharmacy review board" before a they can prescribe a non-formulary drug. (*Id*.)

Dr. Sarrel proposes to testify regarding the prescribing habits of other physicians. Yet his only basis for offering such generalizations is his claim that he has "traveled the country and talked with other physicians." (Sarrel Rep. at ¶ 50 (Exh. 4).) When asked at his deposition, he could not recall the names of specific physicians he had spoken with on this topic. (Sarrel Dep. at 265 (Exh. 3).) Dr. Sarrel could not even recall the names of the managed care plans with which any of these physicians was affiliated. (*Id.*)

Dr. Sarrel should not be permitted to offer testimony on the prescribing habits of other physicians. Although Dr. Sarrel may have expertise on certain medical issues, he has no claim to expertise on the prescribing habits of other physicians. He has not conducted a formal survey of physicians on this topic, and he concedes that he has not reviewed any academic literature on formulary issues. Moreover, Dr. Sarrel's *personal* experience belies his statements concerning the prescribing habits of *other* physicians: although he claims that physicians are generally constrained to prescribe only those drugs

that are on formularies, he concedes that he has long been free to prescribe (and does prescribe) whichever drug he chooses. (Sarrel Rep. ¶¶ 50-51 (Exh. 4); Sarrel Dep. at 98, 264, 267 (Exh. 3).)

Dr. Sarrel should not be permitted to hold himself out as an expert regarding the impact of formulary management on the prescribing practices of other physicians. Courts have excluded similar expert testimony where the witness merely opines on the general practices, experiences or opinions of others. In *United States v. Kelley*, 6 F. Supp. 2d 1168, 1184-85 (D. Kan. 1998), the court excluded expert testimony on the "general practices of outdoor marijuana growers" because the only basis for the expert's testimony was that he had "talked with 'many' outdoor [marijuana] growers . . . ." *See also United States v. Carswell*, 922 F.2d 876, 879 (D.C. Cir. 1991) (excluding testimony of expert who, "[i]n essence, . . . claim[ed] to have been an observant person who was employed in activities that might have enabled a keen observer to learn something about the subjects at issue in this case."); *Sawyer v. Southwest Airlines Co.*, 243 F. Supp. 2d 1257, 1269 (D. Kan. 2003) (expert may not testify about the "sensitivities of African Americans born before 1960" where "[a]bsent proof of a study, polling or testing, [expert's] testimony appears to be speculative and a mere expression of personal views and perceptions.").

Quite simply, Dr. Sarrel is not an expert on either managed care formularies or the prescribing practices of other physicians. His testimony on these topics should be excluded.

CONCLUSION

Plaintiffs intend to call Dr. Sarrel to testify at trial on a number of topics about which he has no expertise. His speculation about the general prescribing practices of physicians throughout the United States, his unsupported suppositions on the source and variability of Premarin pills, and his unfounded and facially incorrect opinions on the dissolution characteristics of Premarin and Cenestin should not be introduced under the guise of expert testimony. Accordingly, the Court should grant Defendants' motion to exclude Dr. Sarrel's testimony on these three subjects.

Dated: May 13, 2005

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned, an attorney, hereby certifies that a copy of the foregoing Motion To Prohibit Plaintiffs From Introducing Certain Evidence Based On The Testimony Or Analysis Of Phillip Sarrel and Memorandum In Support thereof has been served electronically on all counsel of record with CM/ECF Registration on this 13th day of May, 2005, and by regular U.S. mail, postage prepaid upon the following:

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